

REMARKS AND ARGUMENTS

Claims 1-60 are presently pending in this application. Claims 1, 2, and 8-51 are amended herein. Claim 48 is amended and now provides the proper antecedent basis for the terms X1 and X2. Support for this amendment can be found in the specification and in claim 2. Claims 1, 2, and 8-51 have been amended to correct minor errors, including the proper use of the connectors "and" and "or" and the addition of the phrase "in need of treatment". Support for these amendments can be found in the specification and claims as filed. No new matter has been added by these amendments.

Applicants request the addition of new claims 55-60. Support for these claims can be found in claims 49 - 54. No new matter has been added by these claims.

35 U.S.C. §112 First Paragraph

The Examiner has rejected claims 1 and 48-54 under 35 U.S.C. 112, first paragraph, stating that the specification, while being enabling for L representing a group of Formula VA or VB, does not reasonably provide enablement for any linker for the reasons set forth in the Office Action of August 12, 2004. The Examiner further states that the specification fails to provide a specific definition of a linker molecule, and notes that on page 12 of the specification it is stated that L represents the structures VA or VB and that other groups can be used, which are not limited to linkers known in the prior art, and that it would therefore take an undue amount of experimentation to determine what additional linker molecules will be useful in the claimed compounds.

This rejection is respectfully traversed. Claim 48 only is amended herein and is directed to compounds having a linking group of Formula IV. With respect to claim 1 and the claims dependent on it, Applicants submit that one of ordinary skill in the art is able to practice the full scope of the claimed invention described by these claims. See *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). "That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and

perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art.” *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

The use of linkers (or “spacers”) to link two parts of a conjugate was well known at the time the priority application was filed, in July 2002. Therefore, unlike nascent technology, enablement for linker technology does not have to be included within the specification because a person of ordinary skill in the art is familiar with linkers and will have knowledge of linkers independent from the patentee’s instruction. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247 (Fed. Cir. 2004).

Evidence that linkers are well known and understood in the art can be found by looking at similar U.S. patents. In a survey of patents using either the term “linker” or “spacer” in the claims, we retrieved 416 patents having composition, compound, delivery, or agent in the title.¹ Of the first 15 patents related to the chemical arts retrieved, 9 defined the spacer or linker used and 6 did not.² Therefore, 40% of the patents (including the 20 issued most recently from applications prior to July 2002, and therefore subject to the current examination standards of the PTO) did not particularly define the linker or spacer in the broadest linker claim nor provide disclosure or enablement of all possible linkers in the specification. The relevant broad claims or claim sections of these patents are duplicated and presented collectively in Exhibit A. For example, U.S. Pat. 6,790,827 contains claim 24 directed to a method where the bioactive agent of claim 1 “is covalently bound indirectly to the cobalt atom of the organocobalt complex via a spacer.” U.S. Pat. 6,787,517 claims an agent “wherein the therapeutic component and the targeting ligand are attached to each other through a spacer component” in claim 31.

¹ Search performed at the USPTO Web site: (((ACLM/“a linker” OR ACLM/“a spacer”) AND (((TTL/composition OR TTL/compound) OR TTL/deliver\$) OR TTL/agent)) AND APD/19800101->20020701): Hits: 416 patents.

² The 6 patents are:

6,821,632 Composite of a vulcanizable rubber composition and cured rubber product
6,790,827 Bioconjugates and delivery of bioactive agents
6,787,517 Agent and methods for treating pain
6,783,819 Crown compound modified silica coatings for ink-jet media
6,777,237 Bioconjugates and delivery of bioactive agents
6,776,976 Bioconjugates and delivery of bioactive agents

Since the use of a broadly defined linker or spacer group was well-understood at the time this application was filed (as it was for these earlier-filed patents listed in footnote 2), the specification does not have to detail every possibility of the claimed linker to be enabling. Applicants therefore respectfully request reconsideration and withdrawal of this rejection. Nor do applicants ascribe to the activity or any other beneficial property of the claimed conjugates to the linker used to connect the two moieties. Thus, all a person of ordinary skill would have to do is device a linker that would react with and connect the macrolide moiety and the other NSAID moiety. It is submitted that this can readily be done in multiple ways with the exercise of a modicum of ordinary skill.

35 U.S.C. §112 Second Paragraph

The Examiner has rejected claims 2 and 5-54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner has rejected claim 2 as indefinite, stating that a sugar moiety of Formula III is in the wrong place, and that the terminology “Rx may be” in claim 2 renders the claim indefinite since it fails to limit the definition of Rx to the groups set forth. Applicants have amended claim 2 to recite “Rx is” and have moved the sugar moiety to the proper location. Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner further states that the terminology “and pharmaceutically acceptable salts thereof in claims 8-47 is an improper Markush terminology, and that such terminology as “or a pharmaceutically acceptable salt or solvate thereof” can be used to overcome the rejection. Claims 8 – 47 as well as claim 49 have been amended and recite a proper alternative limitation. Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner states that claim 48 is improper in that it contains a period in the middle of the claim, and that it is not clear from claim 48 what the steroid structure on page 35 represents. The Examiner further states that claim 48 is indefinite in that the preamble of the claim reads on preparation of all compounds of Formula I, while the reaction steps presented in the claim are

limited to the preparation of a limited number of compounds, and that there is no antecedent basis in the structural formula I for the variables X2 and X1 in the claim. Claim 48 has been amended to recite proper antecedent basis. Claim 48 has also been amended to remove the period and clarify the relationship of the steroid structure on page 35. Applicants, while not agreeing that claim definiteness requires that the claim preamble be limited to the scope of the claim, find this rejection moot since claim 48 is limited to compounds having linkers of Formula VA or VB. Applicants respectfully request reconsideration and withdrawal of these rejection.

The Examiner states that the terminology "administering to a subject" in claim 50 is unclear as to whether said subject is in need of treatment. Claim 50 has been amended to more clearly claim the invention and claims "administering to a subject in need of treatment." Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner further states that it is not clear from claims 50 and 51 if all the diseases listed are treated at the same time or separately, that the use of the term "or" instead of "and" can be used to overcome the rejection. Claims 50 – 51 have been amended to include the term "or" instead of "and." Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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